507 Eugenia Avenue
Madison 5, Wis.
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Dear Joe:

Well, we've just gotten back! There's no point repeating that our trip was a stimulating experience, some of it enjoyable in a simple sense, some of it (like the Indian refugee slums in Calcutta) almost traumatically distasteful, but part of the world we inhabit— or that being home has its pleasures too, though I do shudder at the pile of work ahead for the next several months.

Your letter of November 1 graced my return. Thanks to you and Amel for the item in the last paragraph. I hope my services will be as worthwhile to you and the Company, in the long run, as the task has been provocative and interesting to me.

There are a number of things I want to talk to you about, and as you will probably find it inconvenient to travel out here (though I hope you will sometime, so we can exchange kodachromes at 30 paces) I will try to manage a trip to Syracuse. I have to go to NY for a Harvey Lecture (which will probably be mainly on L forms etc) on December 19, and I wonder if it would be convenient if I visited you on the 20th or 21st? If you can say yes, I will do my best to manage it, but I better had not make a definite commitment just yet, till I see what's awaiting me at the lab.

I'd send you a record on this, but I have a spot of laryngitis.

Which reminds me: you do have a technical librarian who can do literature searches etc., don't you? My expectation is based on Naomi Cohn's description of her job before she came to Wisconsin— she has, by the way, gone to the Rocky Mountain Rickettsia Lab of the PHS. Anyhow there are a couple of items that might be worthwhile surveying in preparation for our discussion, to wit:

1. There's a fad in vogue in Australia just now for treating colds with very large doses of ascorbic acid. I don't know if there's anything in it, but the first time I've had an unmistakable nasal cold abort was under the regime. Can you find out whether they have been any clinical trials— there must have been with all the fuss about lemon juice a few years ago. (I have to add that I used up the bottle en route and haven't troubled to replace, so my present voicelessness doesn't speak against the case.) This is probably just nonsense, but

2. While thinking (en route from Bombay to Rome) how such a regime could possibly work, I remembered a note by McCarty on the inactivation of pneumococcal DNA by ascorbic acid—which turned out, of course, to be connected somehow with the oxidation of ascorbic to dehydroascorbic, and the concomitant release of H_2O_2. Well, this would hardly account for the effectiveness of a systemic dose, but it did suggest a notion that your unethical congeners in Bristol-Myers might want to explore, namely "BRISTOMINTS" which would be Life-Savers in which some of the citric acid is replaced by ascorbic. Presumably, they could at least do no harm, and someone with a cold or throat irritation wants something to suck on anyhow. I do have some lingering doubts whether peroxides, being mutagenic, might be chronically harmful, but with the ubiquity of catalase, this seems remote

—what I'm concerned about, of course, is possible carcinogenesis; this is farfetched, but ought to be looked for.

Now, McCarty (Je Exp. Med. 81:501-514) does quote a couple of other inactivations by ascorbic + oxygen; I have a suspicion there may be more data particularly for bacteria, and this would be worth having looked up, or even tried out. A point to stress is that traces of Cu catalyse the reaction; I wouldn't advocate putting in Cu, but there might be enough in your commercial grade citric anyhow. If not, ₱/ Fe^{++} might do. (Don't tell this to your ad-men, but think of it: the first scientific coughdrop: vitamin, antibiotic and iron for the blood too!) A girl here, Miriam Selagi, did her Ph.D. thesis, as a matter of fact, on the Cu catalysis, and I can look this up if the project merits any more attention.

What I would stress is that McCarty found ascorbic acid to be rather more potent than added H_2O_2; at the very list, the Bristamint would furnish a slow continuous output.

I've buried what I thought should be 'researched' in the last paragraphs: the →→ marks it.

As long as we're on peroxide and local antibiosis, do you know if notatin (glucose oxidase) would have any application in a similar context? Here you'd start out with a neutral mint, and let gluconic acid furnish the acid taste! Antibiosis by notatin may give some notion of what peroxide can do.

Aside from respiratory infection, the other selling point for a (harmless!) antibiotic mint would be to counteract the presumed cariogenic effect of the sugar.

I would be rather distressed if (as is hardly likely) this notion is exploited without some scientific justification, but there is at least some chance of it, and it should take no great effort to get a at least an in vitro basis, either from the literature or in your own lab.

Needless to say, this diversion is not what I mainly want to discuss with you: on the agenda ought to be (so you can remind me)

virus and tumor chemotherapy
'substitution chemotherapy'
two-stage & continuous fermentation technique (or, how to get rid of unwanted trace metals, maybe)

Yours, as ever,

Joshua Lederberg